REMARKS

1. *Status of the Claims*

Claims 2-16, 22-31, 33, 38-40 and 42-45 are pending.

Claims 2, 16, 33, 42, 43, and 45 are amended herein.

Claim 44 is canceled by this amendment.

No new matter is introduced.

Reconsideration is respectfully requested.

2. *Amendments to the Specification*

The Applicants have noted several typographical errors and informalities, which Applicants have corrected in this Amendment. In the specification, clauses beginning on page 5, line 3 and on page 22, line 24 and paragraphs beginning on page 27, line 12, on page 30, line 6, on page 64, line 14, and on page 77, line 8 have been amended to correct minor editorial problems. The Applicants apologize for these errors.

3. *Amendments to the Claims*

Applicants have also noted some typographical errors and informalities in the claims which are corrected by this Amendment. In claim 2 under clause (m) and claim 33 under the definition of R^3(t), the first instance of "cycloalkylalkynyl" has been replaced by "cycloalkylalkenyl" to correct a typographical error. In claim 16, an extra ";" has been removed prior to the definition of R^3(a). In claim 33, an extra "," has been removed under the definition of R^3(w). In claim 16 under the definition of R^3(f) and claim 42, "heteroaryl selected from" has been removed and in claim 16 under the definition of R^3(g), "substituted phenyl selected from" has been removed because these elements are not presented in "formal" Markush format.

4. *Rejections Under 35 USC 112, Second Paragraph*

The Examiner rejected claims 16, 22-31, and 42-45 as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention.

a. "And"

The Examiner pointed out that in claim 16, under the definitions of R^4, R^5 and R^6, the "and" before the last substituent listed in each of the variable definitions should be changed to "or". Claim 16 has been amended to make this correction.

b. Period

The Examiner pointed out that claims 43 and 44 do not conform to M.P.E.P. 608.01(m) since each claim must end with a period. Claim 43 has been amended to make this correction. Claim 44 has been canceled to reduce issues for appeal.

c. Lack of Antecedent Basis for "The compound of claim 28"

The Examiner pointed out that claims 44 and 45, which each claim "The compound of claim 28", lack antecedent basis from claim 28 which is a method claim. Claim 44 has been canceled to reduce issues for appeal. The Applicants have amended the preamble of claim 45 to recite a method claim instead of a compound claim.

The Applicants believe, in view of the amendments noted above, that all of the Applicants' presently pending claims meet the criteria of 35 USC § 112, second paragraph.

5. *Double Patenting*

The Examiner rejected claims 2-6, 16, 22-24, 33 and 38-40 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 of U.S. Patent No. 6,376,527. The Examiner re-iterated previous bases for rejection, stating, *inter alia*,

that although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims in the patent differ only by generic description of the pyrazole product used in the method.

The Applicants respectfully traverse the rejection of claims 2-6, 16, 22-24, 33 and 38-40. In the Office Action dated July 16, 1999 with regard to the initial application for U.S. Patent No. 6,376,527, the Examiner subjected the pending claims to a restriction requirement to elect a single disclosed species which is patentably distinct. With respect to the restriction requirement, the Applicants' previous offer to file a terminal disclaimer when all outstanding issues were resolved was made in error. The instant application is a division of U.S. Patent No. 6,376,527 and therefore has the same priority and expiration dates. The third sentence of 35 USC §125 provides that

> "A patent issuing on an application with respect to which a requirement for restriction under this section has been made, or on an application filed as a result of such a requirement, shall not be used as a reference against a divisional application or against the original application or any patent issued on either of them, if the divisional application is filed before the issuance of the patent on the other application."

The instant application was filed prior to issuance of US 6,376,527 which the Examiner has sited as the basis for rejection. Thus, Applicants respectfully submit that the claims are fully patentable over claims 19-21 of U.S. Patent No. 6376527, that rejection of Applicants' claims based on this reference is improper, and that no terminal disclaimer is required.

6. *Rejections Under 35 USC §103*

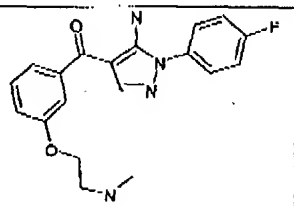
The Examiner rejected claims 2-7, 12, 33 and 38-40 under 35 USC §103(a) as being unpatentable over Faraci et al., WO 94/13643 (US 5712303). The Examiner re-iterated previous bases for obviousness rejections, stating, *inter alia*, that the difference between the teachings of Faraci et al. and Applicants' invention was that of generic description of the products being administered for the intended use.

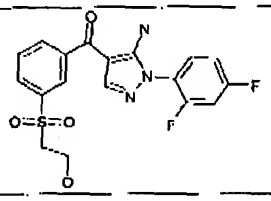
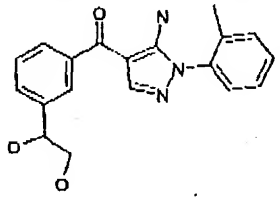
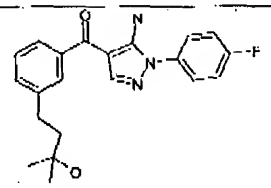
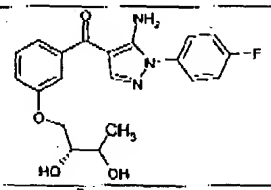
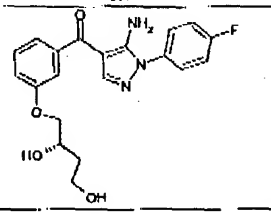
The Applicants respectfully traverse the rejection of claims 2-7, 12, 33 and 38-40 over Faraci et al. A *prima facie* case of obviousness requires, *inter* alia, some suggestion or motivation in the prior art to modify a reference, and a reasonable expectation of success from

making such a modification. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). The Applicants request withdrawal of the rejection under 35 USC §103(a) in view of the results disclosed by Applicants in Table 1 below that are entirely unexpected from the teachings of Faraci et al. In a side by side showing, compounds administered in the instant method of use and structurally similar to those taught by Faraci are effective at inhibition of p38 MAP kinase and the *in vitro* inhibition of TNF alpha production but inactive at inhibition of CRF1. CRF inhibition as shown in Table 1 was determined using the procedure reported in Example 14 of commonly owned patent application US 20040110815. Faraci et al. discloses compounds useful as CRF1 inhibitors, and according to the teachings of Faraci et al. as interpreted by the Examiner, one skilled in the art would reasonably expect that Applicants' compounds should also be CRF1 inhibitors. The lack of CRF activity in Applicants' compounds is thus unexpected in view of the teachings of Faraci et al. Thus compounds used in the instant claimed method show unexpected, beneficial and superior results over the compounds taught in Faraci et al. and the instant claimed invention would not have been obvious to one skilled in the art.

Accordingly, the Applicants request that the Examiner's rejection of claims 2-7, 12, 16, 22-24, 33-35 and 38-41 under 35 USC §103 as unpatentable over Faraci be withdrawn.

Table 1. Pyrazoles Administered in the Instant Claimed Method and Structurally Similar to those taught by Faraci.

#	Structure	Name	P38-MAP-KINASE-IC50 (uM)	TNF-BIOSYNTH IC50 (uM)	% Inhibition CRF1 @ 10 uM
1		[5-Amino-1-(4-fluoro-phenyl)-1H-pyrazol-4-yl]-[3-(2-methylamino-ethoxy)-phenyl]-methanone hydrochloride	1.77	5.02	-2

2		[5-Amino-1-(2,4-difluoro-phenyl)-1H-pyrazol-4-yl]-[3-(2-hydroxy-ethanesulfonyl)-phenyl]-methanone	2.42	5.02	5
3		(5-Amino-1-o-tolyl-1H-pyrazol-4-yl)-[3-(1,2-dihydroxy-ethyl)-phenyl]-methanone	3.265	14.1	-3
4		[5-Amino-1-(4-fluoro-phenyl)-1H-pyrazol-4-yl]-[3-(3-hydroxy-3-methyl-butyl)-phenyl]-methanone	0.5785	6.59	-6
5		[5-Amino-1-(4-fluoro-phenyl)-1*H*-pyrazol-4-yl]-[3-((R)-2,3-dihydroxy-butoxy)-phenyl]-methanone	0.127	0.336	0
6		[5-Amino-1-(4-fluoro-phenyl)-1*H*-pyrazol-4-yl]-[3-((S)-2,4-dihydroxy-butoxy)-phenyl]-methanone	0.149		7

7. *Amendments to Claim 16.*

The Examiner indicated that claim 16 was not allowable because the definition of R^3 was of a broader scope than the R^3 definition in claims 8-11, 13-15 and 25-31 due to obviousness-type double patenting rejection and the rejection under 35 USC 112, second paragraph. Applicants have amended claim 16 to conform the definitions or R^3 to those of allowed claims 8 and 13. The Applicants believe, in view of the amendments noted above, that claim 16 is allowable.

8. *Claim Objections*

The Examiner noted that claims 8-11 and 13-15 were objected to as depending upon a rejected base claim but would otherwise be allowable. Claims 8-11 and 13-15 depend from claim 33 either directly or indirectly, and are believed to be allowable in their present form for the same reasons as base claim 33.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-354-7540.

No fees should be due. However, in the event it is determined that a fee is due, please charge same to Deposit Account No. 18-1700.

Respectfully submitted,

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